IN THE SPECIFICATION:

Please amend the paragraph bridging pages 4 and 5 as follows:

NF-κB binds exclusively to the kappa light chain gene enhancer (the sequence TGGGGATTCCCA (SEQ ID NO: 1)). Initial work provided evidence that NF-kB is specific to B-lymphocytes (B-cells) and also to be B-cell stage specific. NF-κB was originally defected because it stimulates transcription of genes encoding kappa immunoglobulins in B lymphocytes. As described herein, it has subsequently been shown that transcription factor NF-κB, previously thought to be limited in its cellular distribution, is, in fact, present and inducible in many, if not all, cell types and that it acts as an intracellular messenger capable of playing a broad role in gene regulation as a mediator of inducible signal transduction. It has now been demonstrated that NF-κB has a central role in regulation of intercellular signals in many cell types. For example, NF-κB has not been shown to positively regulate the human β-interferon (β-IFN) gene in many, if not all, cell types. As described below, it is now clear not only that NF-κB is not tissue specific in nature, but also that in the wide number of types of cells in which it is present, it serves the important function of acting as an intracellular transducer of external influences. NF-κB has been shown to interact with a virus inducible element, called PRDII, in the β-IFN gene and to be highly induced by virus infection or treatment of cells with double-stranded RNA. In addition, NF-κB controls expression of the human immunodeficiency virus (HIV).

On Page 10, please amend the third through fifth complete paragraphs as follows:

Figure 3 (SEQ ID NO: 23) shows the results of DNase I foot printing analysis of factor-DNA complexes.

Figure 4A (SEQ ID NOS: 24-26) shows the nucleotide sequences of actual and putative binding sites of IgNF-A; Figure 4B is an auto-radiograph of binding assays with various DNA probes of three Ig transcriptional control elements.

Figure 5A (SEQ ID NO: 27) shows the DNA sequence of the promoter region of MODC41; Figure 5B shows an auto-radiograph of RNA transcript generalized in whole cell extracts made from human B lymphoma cell lines RAMOS and EW and from HeLa cells from the indicated templates.

On Page 11, please amend the fifth complete paragraph as follows:

Figure 11A and 11B show location of binding sites in μ50 and μ70 by the methylation interference technique; Figure 11C (SEQ ID NOS: 28-29) provides a summary of these results.

On Page 12, please amend the first through seventh complete paragraphs as follows:

Figure 16 (SEQ ID NO: 30) shows the λgtll-EBNA-1 (λEB) recombinant and the oriP probe.

Figure 17 (SEQ ID NOS: 31-37) shows the sequence of the DNA probe used to screen for an H2TF1 and NF-κB expression.

Figure 18A (SEQ ID NOS: 38-40) shows the nucleotide sequence of the oct-2 gene derived from cDNA and the predicted amino acid sequence of encoded proteins.

Figure 18B (SEQ ID NOS: 41-43) shows the nucleotide sequence of the 3' terminus and predicted the amino acid sequence of the C-terminus derived from clone pass-3.

Figure 18C is a schematic representation of the amino acid sequence deduced from oct-2 gene derived cDNA.

Figure 19 (SEQ ID NO: 57) is a schematic representation of expression plasmid pBS-ATG-oct-2.

Figure 20 (SEQ ID NOS: 44-51) shows amino acid sequence alignment of the DNA binding domain of oct-2 factor with homeo-boxes of several other genes.

On Page 13, please amend the first complete paragraph as follows:

Figure 25 (SEQ ID NOS: 52-53) is a representation of binding sites for the NF-kB transcription factor in the immunoglobulin kappa light chain enhancer and the HIV enhancer. Boxes indicate the binding sites for NF-kB (B); other regulatory sites are referred to as E1, E2 and E3 and Spl. Dots indicate guanosine residues in the kappa enhancer whose methylation interfered with binding of NF-kB.

On Page 19, please amend the second complete paragraph as follows:

Figure 39 (SEQ ID NOS: 54-56) is a diagram showing the location of positive regulatory domain II (PRDII) within the interferon gene regulatory element (IRE) and a comparison of the nucleotide sequences of the PRDII site, KB site, and the H2TF1 site.

On Page 22, please amend the third complete paragraph as follows:

Figure 43 (SEQ ID NOS: 58-59) is the nucleotide sequence and the amino acid sequence of IkB-α.

Please amend the paragraph bridging pages 27 and 28 as follows:

NF-κB (previously referred to as Kappa-3) binds only to the Ig light chain enhancer. The binding is mediated by the sequence TGGGATTCCCA (SEQ ID NO: 60). The factor initially was characterized as lymphoid cell specific and also as lymphoid stage specific; that is, work showed that it is expressed only by mature B-cells. Thus, it is a marker of B cell maturation (e.g. the factor can be used to type B cell lymphomas). Additional work, described in Examples 8-15 in particular, has shown that NF-kB is an inducible factor in cells, both pre-B and non pre-B, in which it is not constitutively present (Example 8), that it is present in the cytoplasm as an inactive precursor (Examples 10 and 11), and that the inactive precursor is a complex of NF-kB and an inhibitor, referred to as IkB, which converts NF-kB to an inactive form in a reversible saturable and specific reaction. Dissociation of the complex results in activation of NF-kB (appearance of NF-kB binding activity) and translocation of the NF-kB into the nucleus.

Please amend the paragraph bridging pages 83 and 84 as follows:

For example, the sequences of the κ immunoglobulin enhancer, the SV40 70 base pair repeat, the HIV long terminal repeat, the MHC class I H2-kb gene and the interferon β PRDII

gene, all possess NF-κB binding sites (Table 2). By comparing sequences to which NF-κB binds specifically, a consensus sequence has been determined:

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    C   C
GGGRATYYAC.      (SEQ ID NO : 12)
    T   T
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DNA sequences which flank the binding site are scanned for convenient restriction enzyme recognition sequences to facilitate removal of the fragment from the longer sequence in which occurs and its subsequent insertion into the expression vector. If such sequences are present, the transfer of the fragment carrying the binding site, to the expression vector, is straightforward. If convenient sites do not exist, fragment transfer is facilitated through the introduction of such restriction enzyme recognition sequences using well known, site-directed mutagenic techniques. The construct, prepared as described, can then be introduced into a biological system of interest.

On Page 86, please amend Table 2 as follows:

TABLE 2 Sequences recognized by NF-KB.

Gene	Sequence
Ig κ enhancer - mouse	GGGGACTTTCC (SEQ ID NO: 2)
SV40 enhancer	
HIV-1 (-91)	
CMV (4)[1], [2]	
HIV-1 (-105)	AGGGACTTTCC (SEQ ID NO: 3)
HIV-2	
CMV (1)1	
β2-microglobulin	
serum amyloid A - g9	
Ig κ enhancer - human	GGGGATTTCC (SEQ ID NO: 4)
CMV (3)[1]	
Interferon-β - PRDII	GGGAAATTCC (SEQ ID NO: 5)
CMV(2)[1]	GGGACTTTCC (SEQ ID NO: 6)
MHC class II - E_α^d	GGGACTTCCC (SEQ ID NO: 7)
IL-2 lymphokine	GGGATTTCAC (SEQ ID NO: 8)
mouse tL-2Rα	GGGGATTCCT (SEQ ID NO: 9)
human IL-2Rα	GGGAATCTCC (SEQ ID NO: 10)
MHC class I - H2 - K^b	GGGATTCCCC (SEQ ID NO: 11)
HLA - A2, A11, B7	
B27, B51	
CONSENSUS[3]:	C C GGGRATYYA C (SEQ ID NO: 12) T T

[1] In this particular element. the sequence has not been tested in a binding assay. All others have been proven by direct binding and usually by inhibition of binding to the Ig x sequence.

[2] Since there are four putative NF-KB recognition sites in the cytomegalovirus enhancer, these have been numbered 1-4 as they are found from S' to 3' on the coding strand.

[3] Consensus is based on all sequences though the assignments of the sixth and tenth positions ignore one deviant.

On Page 117, please amend the first complete paragraph as follows:

The binding site of this factor on the *κ3* fragment was localized by methylation interference experiments. In two different extracts, methylation at three of a stretch of 4 residues within this sequence completely abolished binding (Figure 14, compare lane 1 [complex] and 2 [free]; and lanes 3 [complex] and 4 [free]). This stretch of G's forms a part of the conserved region (GGGGACTTTCC (SEQ ID NO: 2)) between the SV40 enhancer and κ3. Thus, the binding site was localized towards one end of the κ3 fragment. The results also served to explain the specific competition observed earlier with the SV40 Enhancer. Interestingly, deletion mapping of the κ enhancer shows that sequences within the κ3 fragment are extremely important for enhancer function.

Please amend the paragraph bridging pages 120 and 121 as follows:

The plasmid pUCoriP1 was constructed by subcloning the EcoRI-NcoI fragment from the oriP region of the EBV genome into the SmaI site of pUC13. This fragment contains 20 high affinity binding sites for EBNA-1. pUCoriP2 was derived from pUCoriP1 by subcloning of an oriP fragment (EcoRI-BstXI) of the latter into the SmaI site of pUC13. pUCoriP2 contains 11 high affinity binding sites for EBNA-1. pUCORIλ2 was made by insertion of a synthetic binding site for the bacteriophase λ0 protein (AAATCCCCTAAAACGAGGGATAAA (SEQ ID NO: 13)) into the SmaI site of pUC13. The complementary oligonucleotides were a gift of R. MacMacken. pUCMHCI and pUCmhcI were constructed by insertion of the following oligonucleotides:

GATCCGGCTGGGGATTCCCCATCT (SEQ ID NO:14)
GATCCGGCTGcGGATTCCCaATCT (SEQ ID NO: 15)
GCCGACCCCTAAGGGGTAGACTAG (SEQ ID NO:16)
GCCGACgCCTAAGGGtTAGACTAG (SEQ ID NO: 17)

into the BamHI site of pUC13. The wild type sequence is a binding site for H2TF1 and NF-κB. pUCOCTA is a similarly constructed pUC18 derivative that contains a synthetic recognition site (ATGCAAAT) for the mammalian octamer binding protein(s). The plasmids

p190H2KCAT (-190 to +5) and p138H2KCAT (-138 to +5) contain 5'-deletions of the H-2K^b gene promoter fused to the coding sequence for chloramphenicol acetyl transferase. All plasmid DNAs were purified by an alkaline lysis protocol followed by two bandings in CsCl-EtBr gradients.

On Page 137, please amend the first complete paragraph as follows:

cDNA's were subcloned from λgtll to pGEM4 (Promega), and these plasmids were used for DNA sequence analysis and in vitro transcription. Plasmid pBS-ATG was kindly provided by H. Singh and K. LeClair and was constructed by ligating a 27 by long oligonucleotide containing an ATG codon surrounded by the appropriate boxes for efficient initiation, TGCACACCATGGCCATCGATATCGATC (SEQ ID NO: 18), into the Pstl site of pBS-/+Bluescropt plasmid (Stratagene). The expression vector pBS-ATG-oct-2 depicted in Figure 19A was designed for transcription and translation in vitro and was constructed by cleaving pBS-ATG with Smal and ligating the blunt-ended EcoRI 1.2 kb cDNA fragment from plasmid 3-1 (position 655 to 1710 in Figure 18A).

On Page 142, please amend the first complete paragraph as follows:

The wild type octamer motif competed efficiently for binding but the octamer motifs containing point mutations either did not compete or competed less well than the wild type motif. In fact, the two mutants which showed slight competition for the binding of the lysogen protein, TCATTTCCAT (SEQ ID NO: 19) and ATATTGCAT, were the only mutants which somewhat competed the binding of NF-A1 and NF-A2 in a WEHI 231 nuclear extract.

On Page 162, please amend the first partially complete paragraph as follows:

This induction phenomenon was not restricted to the 702/3 cell line; another pre-B cell line, PD (Lewis S., et al., Cell 30:807-816 (1982)), was weakly positive for the factor prior to induction (Figure 21B, lane 3; Sen and Baltimore, 1986) but was strongly induced-by LPS (Figure 21B lanes 5,6). A number of other minor bands could be seen in the binding assay, some

of which were inducible and others not. The major inducible band comigrated with the major band produced by B cell and plasma cell extracts (typified by WEHI 231 extracts in Figure 21A, lane 6 and Figure 21B, lane 2). We have earlier characterized this band by competition experiments and localized the binding site of the factor by methylation interference experiments defining the band as one produced by interaction of the NF-KB factor with the B site within the enhancer (a site containing the sequence GGGGACTTTCC (SEQ ID NO: 2)). Thus two pre-B cell lines, one with a rearranged K gene (702/3) and the other in the process of undergoing rearrangement (PD), are clearly inducible by LPS for NF-KB activity.

Please amend the paragraph bridging pages 182 and 183 as follows:

The plasmids p-41βCAT (-41, β), p-41PII4r (-41P(P)), and p-41PΔI2r (-41 β (P)) were constructed as follows: in Fan, C. M. and T. Maniatis, EMBO J., in press (1989). The nucleotide sequence of the PRDIIx2 ($PRDII_2$) is 5'-GATCTGTGGGAAATTCCGTGGGAAATTCCGGATC-3' (SEQ ID NO: 20). The construction of β 56 (c-fosCAT), o56(B)2 (J16), and L56(B) (J32) were described by Pierce et al., Proc. Natl. Acad. Sci. USA, 85:1482-1486 (1988). The KB oligonucleotides were: Wild-type: 5'-TCGACAGAGGGGACTTTCCGAGAGGCTCGA-3' (SEQ ID NO: 21) and mutant: 5'-TCGACAGAATTCACTTTCCAGGAGGCTCGA-3' (SEQ ID NO: 22). The IRE was isolated as a Bg1II-BamHI fragment (Goodbourn et al., Cell, 45:601-610 (1986)) and cloned into pSP73. Mutant PRDII sites were described in Goodbourn, S. and T. Maniatis, Proc. Natl. Acad. Sci. USA, 85: (1988).